REMARKS

Upon entry of the above amendments, this application will contain claims 1-14, 16-19, and 21-23 pending and under consideration. Claim 23 has been amended. Applicants appreciate the entry of the earlier amendments provided; the withdrawal of the rejection of claims 13 and 16 under 35 USC §112, second paragraph; and the withdrawal of the rejection of claims 1-13, 15 and 18 under 35 USC §102(b). For the reasons discussed more fully below it is believed that the claimed invention is patentable over the cited art. Therefore further consideration is requested and withdrawal of all rejections leading to allowance of all claims currently pending in the application is similarly requested.

Rejections Under 35 USC §112

Claim 23 was rejected under 35 USC §112, second paragraph as indefinite. Specifically it was concluded that the language "various levels and gradients types of growth factor" was confusing, making it difficult to determine Applicants' intended meaning. The language objected to has been removed. The amended claim only requires "growth factors." It is believed that claim 23, as amended, is sufficiently definite. Withdrawal of this rejection is requested.

Rejections Under §103

Claims 1-14, 16-19, and 21-23 were rejected under 35 USC 103(a) over Curtis in view of Strathclyde (EP 419234, "Strathclyde") and Hansbrough et al. (US 5,460,939). The Office Action reasserts its previous rejection under Curtis and Strathclyde and currently includes additional arguments regarding Curtis in combination with Hansbrough.

Regarding the combination of Curtis and Strathclyde, Applicants' position in the prior response was that because Curtis et al "...do not disclose or suggest the fiber compositions presently claimed..." the claims in question were patentable over the references cited. In maintaining the rejection under 103(a), the Office Action only partially addressed Applicants' argument focusing on the compositions claimed. Applicants' argument was that Curtis did not disclose or suggest the fiber compositions presently claimed. Applicants' lack of emphasis on

this structural distinction may account for it not being specifically addressed in the current Office Action. Applicants will address this distinction in detail below.

The previous Office Action characterized Curtis as disclosing:

> "...a method of culturing eukaryotic cells (epithelial cells and fibroblasts) on flexible substrates that are sheets with parallel longitudinal grooves and ridges. The sheets may be rolled to form round tubular fibers or folded to form longitudinally split fibers. The sheets may be stacked or formed into any other shape to form the shape needed for a specific anatomical site or surgical procedure. Thus multiple layers or multiple fibers may be used."

Applicants respectfully disagree with this characterization of the material disclosed in Curtis as a fiber for the following reasons. First, Curtis does not characterize his material at any point as a fiber. Had Curtis understood the tubular material to be a fiber, the Curtis specification could have described it as a fiber. The Curtis specification did not describe the tubular material as being a fiber nor did Curtis describe any attributes of the tubular material that would allow one skilled in the art to conclude that a fiber was intended.

Second, the tubular material disclosed by Curtis does not correspond to any definition of "fiber" Applicants have been able to locate. The word "fiber" is defined in Webster's New Collegiate Dictionary, Second Edition (1960), as "a thread or thread-like structure or object." Such thread-like structures typically have a length that is orders of magnitude greater than its cross-section. This description does not correspond to the tubular material disclosed by Curtis. Curtis teaches making sheets of the biodegradable material having grooves by stamping sheets (having the shape of a glass petri dish) of the biodegradable material to form channels on one surface and in certain embodiments folding these sheets over to form tubes (See Example 1(c), page 14 and specification at page 8, last full paragraph). The one example where Curtis's tubular material is used (page 8, second full paragraph) describes inserting "...a central tube within the wound between separated ends of the tendon, together with a tubular sheet of the substrate wrapped around the tendon and tied off around each end with a conventional suture." Folding the sheets taught by Curtis provides tubes having none of the attributes of a fiber.

The Office Action is correct in describing Strathclyde as disclosing a method of culturing cells in which fibers of two different materials are used. However, Strathclyde does not teach how to grow cells on the surface of a fiber. In fact, such growth would interfere with the operation of the cell growth apparatus disclosed by Strathclyde. The fibers used by Strathclyde are contained in membranes designed to provide nutrients and remove waste from the cells being cultured and to exchange gaseous materials needed for continued cell growth. The cell culture apparatus disclosed by Strathclyde is designed to culture cells in a suspended state. Consistent with this purpose, Strathclyde describes cell levels in terms of cells/ml (See Example 1, column 14 lines 2-9). Were cells to adhere to the surface of the membranes in sufficient quantity, their presence would, in fact, interfere with the exchange of materials, the membranes stated function. Example 2 (column 14) provides an example of the serious effects of not being able to remove waste products and exchange gases. Nothing in Strathclyde teaches or suggests the method of any of the currently pending claims.

Additionally, the teaching of Hansbrough et al. neither adds anything to Curtis nor makes up for Strathclyde's deficiencies. Hansbrough describes an external dressing referred to as a living skin replacement. Dermal Fibroblasts are grown within a nylon mesh in contact with a silicon rubber film (See Fig. 1). Nothing in Hansbrough teaches or suggests the advantage of its mesh having at least one open-topped channel in or to which cells can adhere and grow. The use of Hansbrough's dressing is limited to external applications because of the silicone rubber barrier to cells forming connections between layers sandwiched on top of each other.

Finally neither Curtis, Strathclyde, nor Hansbrough teach or suggest how to obtain the advantages provided by the presently claimed method. Curtis teaches a very limited use of multiple layers of his sheets in tubular form. The example discussed above provides for one tube within a second tube where cell growth is promoted initially in a cylindrical manner between tubular surfaces. Otherwise the back side of the sheet forming the tube will initially act as a barrier to cells forming connections between layers. No such barrier exists with Applicants' fiber shaped structures. In contrast to Curtis's tubular structures, Applicants' method utilizing fibers can be used to construct multi-layer matrixes that are used for 3-dimensional growth of replacement tissue. As a result, such a matrix may comprise multiple layers of fibers oriented in

the same direction allowing a 3-dimensional growth of tissue, such as for example, muscle tissue. Alternatively, the matrix may have fibers oriented in different (e.g. perpendicular) directions for use in the formation of a vascular graft or a replacement esophagus. In such replacement tissue, the epithelial cells in the lumen need to be aligned in parallel with the tube-like esophagus and the smooth muscle cells need to be aligned circumferentially around the tube-like esophagus (i.e. perpendicular to the epithelial cells).

The methods of the present invention allow ready construction of matrixes providing cell growth in any required direction. This is a significant advantage with multi-layer matrixes comprised of fibers. Such matrixes allow cells attached to the fibers to connect with cells in other layers above, below or beside them. As a result, the replacement tissue can be constructed having a quality that corresponds to the tissue being replaced.

In contrast, Curtis only discloses flexible flat substrates or sheets with grooves that will provide guided cell growth in a single direction. Additionally, the substrates disclosed by Curtis, whether in sheet form or rolled to form a tube, do not allow ready connection between growing layers of cells in the way provided by the present invention. Layering of the Curtis device, whether in sheet form, tubular form or any other form, results in the formation of a barrier to cells forming connections between at least some of the layers.

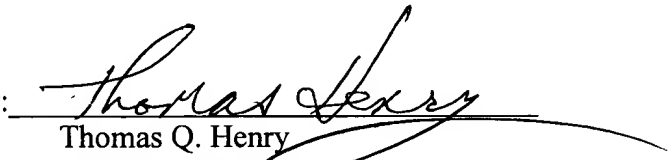
Because the cited references either alone or in combination do not disclose or suggest the fiber compositions presently claimed in independent claim 1 it is believed that claim 1 and claims 1-14, 16-19 and 21-23 are distinct and patentable over the references cited. Reconsideration and withdrawal of all rejections are requested.

Conclusion

In view of the amendment to claim 23 Applicants submit that amended claim 23 complies with 35 USC § 112, second paragraph. Further in view of the foregoing remarks, the Applicants respectfully submit that the cited references, either singly, or in combination, do not make obvious the claimed invention. Accordingly, reconsideration leading to withdrawal of all the rejections under 35 USC §§112and 103(a) and passage of this application containing claims 1-14, 16-19, and 21-23 are respectfully requested. Additionally, because the current application is

under final rejection, the Examiner is invited to telephone the undersigned attorney at the earliest opportunity if there are any questions about this submission or other matters, which might facilitate the resolution of any pending matters.

Respectfully submitted,

By: 

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